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ABSTRACT

This report discusses the outcomes of a study that examined 216 comparably aged children and adolescents (ages 2-18) with fragile X or autism to determine whether longitudinal change in cognitive ability and adaptive behavior was similar in the two groups. Results found decreases in Intelligence Quotient scores in young children with fragile X as well as those with autism. Older children and adolescents with autism exhibited stable test-retest scores, while older children with fragile X continued to show decreases. Comparable declines in adaptive behavior were observed in both groups, at all ages, and across all adaptive behavior domains. (Contains 33 references.) (CR)

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LONGITUDINAL CHANGES IN COGNITIVE ABILITY AND ADAPTIVE BEHAVIOR IN CHILDREN AND ADOLESCENTS WITH THE FRAGILE X MUTATION OR AUTISM

ED 449 607

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ABSTRACT

Early reports of an association between the fragile X (FRAXA) mutation and autism have not been supported by later studies. Despite their differences, individuals with FRAXA or autism have similar aberrant behavior patterns. We examined comparably aged children and adolescents with FRAXA or autistic to determine whether longitudinal changes in cognitive ability and adaptive behavior were similar in the two groups. We found decreases in IQ scores in young children with FRAXA as well as those with autism. Older children and adolescents with autism exhibit stable test-retest scores while older children with FRAXA continue to show decreases. Comparable declines in adaptive behavior were observed in both groups, at all ages, and across all adaptive behavior domains.

INTRODUCTION

Early genetic studies of males with mental retardation (MR) who were also diagnosed as autistic found a proportion expressing the fragile X [FRAXA] mutation cytogenetically (Brown et al. 1982; 1986; Meryash et al., 1982). As a result, many researchers thought there was a strong relationship between FRAXA and autism. Later reports found great variability in the proportion of autistic individuals positive for the FRAXA mutation, ranging from 0% (Venter et al., 1984) to 16% (Blomquist et al., 1985). Einfeld et al. (1989) examined age-matched samples of males with developmentally disabilities and males with FRAXA and found no significant differences in the frequency of autism. They concluded that there was no association between autism and fragile X. A meta-analysis of all studies of autistic MR and non-autistic MR individuals revealed no significant differences between the proportion of FRAXA cases among males with autism and the proportion of FRAXA cases among non-autistic MR males (Fisch, 1992). Subsequent interest in the association between FRAXA and autism waned.

Despite marked differences between the two populations, there is a considerable overlap in aberrant behavior, eg, self-injury and repetitive speech, among non-FRAXA autistic and non-autistic individuals with the FRAXA full mutation. Similarities in their social and communication deficits have been documented elsewhere (Feinstein &

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Reiss, 1998; Dykens & Volkmar, 1997; Baumgardner, Reiss, Freund & Abrams, 1995). Recent studies have shown an interest in longitudinal changes in cognitive ability in youngsters with autism (Lord & Schopler, 1989; Schatz & Hamdan-Allen, 1995; Freeman et al., 1985; 1991; Venter, Lord & Schopler, 1992; Sigman, Ruskin & Arbeile, 1999; Stone et al., 1999) and FRAXA (Fisch et al., 1996; 1999b). Children with autism whose cognitive abilities were evaluated initially between ages 3-6 years were shown to have relatively stable IQ scores when retested as many as 12 years later (Freeman et al., 1985; Lord & Schopler, 1989; Freeman et al., 1991; Sigman, Ruskin & Arbeile, 1999). On the other hand, age-related declines in IQ scores among young males with FRAXA has been well documented (Rogers & Simensen, 1987; Fisch et al., 1991; 1992). Prospective longitudinal studies of children and adolescents with the FRAXA full mutation report decreased IQ scores in nearly all males (Fisch et al., 1996), and in most females (Fisch et al., 1999a). These researchers also noted cohort-specific effects; that is, younger males -- those tested before age 6 years -- showed steeper, more significant declines than those tested after the age of 9, when little or no change occurred.

Curiously, prospective evaluation of adaptive behavior skills among children with autism and adolescents has not been investigated systematically. Jacobson & Ackerman (1990) reviewed adaptive functioning among 1,442 autistic and 24,048 MR individuals. Among children ages 5 to 12 years, individuals with autism displayed superior motoric daily living skills compared to same-aged children diagnosed as MR only. However, differences diminished when older groups were compared, suggesting there may be a plateau effect associated with adaptive behavior skills in individuals with autism. Loveland & Kelly (1988) reported that individuals with Down syndrome demonstrated acquisition of adaptive skills in all domains, while those with autism did not. More recently, however, Schatz & Hamdan-Allen (1995) examined the effect of age and intelligence on children and adolescents with autism and found that adaptive behavior was stable from preschool to adolescence. Using the Vineland Adaptive Behavior Scale (VABS) Freeman et al. (1999) found rates of growth in the Communication Domain and Daily Living Skills were related to initial IQ scores, whereas rate of growth in Socialization skills was not. Among children and adolescents with the FRAXA mutation, nearly all males with the FM (Fisch et al., 1996), and most females with the FM (Fisch et al., 1999a) showed longitudinal declines in adaptive behavior scores.

Lack of systematic change in IQ scores among may be accounted for by the increased variability introduced by a multiplicity of instruments used to measure cognitive ability (Lord & Schopler, 1989; Sigman, Ruskin & Arbeile, 1999; Ventner, Lord & Schopler, 1992) or the breadth of IQ categories used (Freeman et al., 1985; 1989). Similarly, the combination of various age groups evaluated with different IQ tests may interact with one another to mask the effect of age on adaptive behavior scores on autistic youngsters (Schatz & Hamdan-Allen, 1995; Loveland & Kelly, 1988). Therefore, we wished to evaluate the development of adaptive behavior and cognitive abilities in children and adolescents diagnosed as autistic compared with those with the FRAXA

mutation using a single IQ test to measure cognitive ability and a single instrument to measure adaptive behavior. Given the overlap in aberrant behaviors, one could hypothesize comparably aged individuals from these two populations might exhibit similar developmental profiles.

METHOD

Subjects

Two hundred sixteen children and adolescents, chronological age 2-18 years, who participated in a comprehensive study between 1995 and 1998 by the J. C. Self Research Institute for Human Genetics and who received a diagnosis of autism served as one population for our study. Diagnosis of autism was based on the findings from the Autism Diagnostic Inventory - Revised (ADI-R; Lord, Rutter & Le Couteur, 1994) or the Childhood Autism Rating Scale (CARS; Schopler, Reichler & Renner, 1988). All participants diagnosed as autistic were tested genetically and found negative for the FRAXA mutation on Southern blot and PCR. Individuals with autism who demonstrated verbal ability and were capable of achieving above floor levels on the SBFE were tested initially between 3 and 12 years using the SBFE and the VABS (N=18). Scores obtained were compared with individually age-matched, non-autistic males who tested positive for the FRAXA mutation (N=18) and served as controls. Non-autistic, FRAXA males were selected from a population of 46 male children and adolescents evaluated by our ongoing multicenter study of youngsters with the FRAXA mutation.

Materials

A cognitive-behavioral battery consisting of two standardized tests was administered: the Stanford-Binet Fourth Edition (SBFE; Thorndike et al., 1986); and the Vineland Adaptive Behavior Scales (VABS; Sparrow et al., 1984). To determine cognitive ability, all verbal children with autism and all males with the FRAXA mutation were administered the SBFE. The SBFE is a well-standardized instrument used to assess IQ. It has excellent psychometric properties targeted specifically for this age group. The SBFE is normed for individuals ages 2-23 years. Among special populations, overall SBFE composite scores are comparable to WISC-R full scale IQ scores. To determine adaptive behavior levels, parents and caregivers of participants were interviewed using the VABS. The VABS is also a well-standardized instrument tested in children ranging in age from 2 to 18 years. Reliability for the VABS is excellent. The VABS is also well suited for evaluating cognitively impaired and other special populations (Sparrow et al., 1984).

Procedure

All males with the FRAXA mutation were tested and retested with the SBFE and VABS between November 1990 and May 1998. The mean inter-test interval was 2 years

(±0.1 yr). Test-retest results for many of the males with FRAXA in this study have been previously published (Fisch et al., 1996). All verbal autistic individuals were tested and retested with the SBFE and VABS between November 1986, and September 1997. The inter-test interval for autistic individuals was 2.7 years (±1.6 yr).

RESULTS

Cognitive Abilities

To determine whether there were cohort-specific effects, individuals with autism and FRAXA controls were separated into 2 age groups: [1] those individuals tested initially before the age of 6 years (N=8 in each group); [2] those tested for the first time at or after age 6 years (N=10 in each group). Test-retest IQ scores are presented in Figure 1. Test-retest scores for individuals with FRAXA exhibit marked declines in both age groups, as reported previously (Fisch et al., 1996).

To determine whether longitudinal changes in IQ scores were statistically significant, test scores were analyzed using a repeated measures multiple analysis of variance (MANOVA; SPSS Advanced Models 9.0, 1999) with Group (FRAXA or autistic) and Cohort (less than 6 years, more than 6 years) as independent variables. Output for the model indicates significant within-subjects and between-subjects effects (See Table 1).

Repeated measures analysis shows significant declines in IQ scores irrespective of Group or Cohort ($F=26.20$, $p<.0001$). Decreases in IQ scores were also significant within each age Cohort ($F=16.64$, $p<.0001$) and within each Group ($F=7.22$, $p<.01$). Older children manifested significantly lower scores than younger children ($F=5.06$, $p<.03$). Post hoc analyses revealed mean IQ scores for children with FRAXA in the younger cohort were initially in the mild range (Mean initial IQ=63.3 ± 1.9), but on retest declined significantly (Mean retest IQ=50.4 ± 2.5; paired $t=-8.84$, $p<<.001$). For the older cohort with FRAXA, mean IQ scores also declined significantly, from a mean initial IQ=48.0 (±2.6) to a mean retest IQ=42.1 (±2.4; paired $t=-6.22$, $p<<.001$). IQ scores for the younger cohort of children with autism also showed significant declines. IQ scores declined from an initial mean IQ=52.3 (±4.1) to a retest mean IQ=43.0 (±1.9; paired $t=-2.36$, $p<.05$). In the older group of children with autism, no significant changes in IQ score were recorded (Mean initial IQ=45.8 (±2.9); mean retest IQ=49.2 (±3.7): $t=1.33$, p=ns).

To determine whether these patterns were reflected in the standard area scores (SAS) that form the SBFE composite IQ, we examined test-retest SAS scores in Verbal Reasoning, Abstract/Visual Reasoning, and Short-term Memory in these subjects. Quantitative Reasoning was excluded from analysis as too many subjects were unable to complete items on this subtest. Significant repeated measures MANOVA of SAS scores are shown in Table 2.

Results indicate significant differences in all SAS areas. In Verbal Reasoning, within-subject retest scores decreased significantly irrespective of Group or Cohort ($F=45.45$, $P<<.001$). There were also significant differences between the autistic and FRAXA Groups in Verbal SAS scores ($F=10.42$, $p<.003$). Age Cohorts showed only marginal differences ($F=3.70$, $p\sim.06$). In Abstract/Visual Reasoning, there were significant within-subject declines, both within each age Cohort ($F=4.54$, $p<.04$) and within each Group ($F=4.57$, $p<.04$). Short-term Memory also showed significant within-subject decreases in SAS scores, irrespective of Cohort or Group ($F=4.44$, $p<.04$). There were only marginal differences between age Cohorts ($F=3.82$, $p\sim.06$). in all SAS areas, children and adolescents with FRAXA exhibited steeper decreases than did age-matched children with autism.

Adaptive Behavior Levels

Results from adaptive behavior composite (DQ) scores are presented in Figure 2. DQ scores for both groups and both cohorts show declines from initial examination to retest. Not unexpectedly, the autistic group exhibits lower DQ scores than the FRAXA group, and for both younger and older cohorts.

To determine the statistical significance of longitudinal changes in DQ Composite scores and Domain scores were also analyzed using repeated measures MANOVA (SPSS Advanced Models 9.0, 1999) with Group and Cohort as additional independent variables. Output for the model is shown in Table 3.

Analysis reveals significantly lower within-subject retest Adaptive Behavior Composite scores, irrespective of Group or Cohort ($F=24.51$, $p<<.001$). Moreover, the group with autism manifested significantly lower Composite scores compared to the group with FRAXA, regardless of age Cohort (13.05, $p<.001$).

Analysis of Domain scores indicates significantly lower within-subject retest Communication scores, Group or Cohort notwithstanding ($F=17.27$, $p<<.001$). Despite problems in both expressive and receptive language in both groups of subjects, Communication Domain scores in the group with autism are significantly lower than among individuals with FRAXA ($F=8.84$, $p<.006$). Scores were also significantly lower between age Cohorts ($F=3.94$, $p<.05$). Daily Living Skills show significantly lower retest scores, regardless of Group membership or age Cohort ($F=35.65$, $p<<.001$). Daily Living Skills were significantly lower among the group with autism when compared to the group with FRAXA ($F=9.61$, $p<.004$), and were significantly lower in the older Cohort compared to the younger one ($F=4.26$, $p<.05$). Socialization Domain retest scores were also significantly lower, irrespective of Group or Cohort ($F=8.99$, $p<.005$). Not unexpectedly, the group with autism had significantly lower Socialization scores compared with the group with FRAXA ($F=27.57$, $p<<.001$). Unlike IQ scores, children and adolescents with autism exhibit declines in all domain scores comparable to those manifested by children with FRAXA.

SUMMARY AND DISCUSSION

As measured by IQ score, young verbal children with autism initially exhibit lower intellectual abilities than do same-aged children with the FRAXA mutation. Like young children with FRAXA, young children with autism manifest declines in IQ scores. Unlike children with FRAXA children, older children with autism attain a plateau in IQ scores, while same-aged children with the FRAXA mutation continue to exhibit declines. These findings support results obtained previously (Freeman et al., 1985; Lord & Schopler, 1989; Ritvo et al., 1989; Freeman et al., 1991; Sigman, Ruskin & Arbeile, 1999) in which individuals with autism demonstrated age-related stability in IQ scores. Among older children with autism in this study, stable test-retest scores were found in several areas of reasoning: verbal ability, abstract/visual skills, and short-term memory. Unlike the results obtained by Schatz & Hamdan-Allen (1995), Freeman et al. (1999) and Bailey et al. (2000) we find children with autism show declines in adaptive behavior scores very much like their FRAXA counterparts. The difference in outcomes may be due in part to the use of age-equivalent (AE) scores as opposed to standardized scores to detect test-retest differences. Fisch et al. (1999b) found Domain AE scores for the VABS were more variable than standard scores, obscuring observed mean differences. In addition, they found small differences in raw scores produced large differences in age equivalent scores.

Unlike cognitive ability, declines in all domains of adaptive behavior -- Communication, Daily Living Skills, and Socialization -- were observed among children with FRAXA as well as those with autism, in both age cohorts. Although it may seem like regression in abilities, this is not the case. Declines in adaptive behavior scores reflect the fact that these children acquire adaptive behavior at a slower rate than do their age-mates. Consequently, children with autism or FRAXA fall further and further behind their cohort as they grow older. A secondary hypothesis could include a premature arrest in acquisition of skills.

Studies of longitudinal changes of individuals from FRAXA and autistic populations have important implications for caregivers and educators of children with special needs. In particular, although it is important to provide children with developmental disabilities various cognitive tasks to enhance problem-solving abilities, it is equally important to equip them with the adaptive behavior skills they will need for self-maintenance as they become adults who are not longer living with their parents. Individuals with developmental disabilities who lack the skills to communicate to others, who are unable to care for themselves daily, and who are severely deficient in relating to others will have great difficulty living independently and adjusting to a workplace environment (Rumsey, Rapaport & Sceery, 1985). A prospective study designed to assess long term stability in adaptive behavior in autistic individuals is in progress.

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Table 1. Repeated Measures Analysis of IQ Scores for Children with FRAXA and Autism

	Variable	df	Mean Square	F-Ratio	Signif. Level
Within Subjects					
	Time	1	673.8	26.20	<.0001
	Time w/in Cohort	1	427.9	16.64	<.0001
	Time w/in Group	1	185.6	7.22	<.01
	Residual	32	25.7		
Between Subjects					
	Cohort	1	628.1	5.06	<.03
	Residual	32	124.1		

Note: Factors not shown in the table were not statistically significant.

Table 2. Repeated Measures Analysis of Test-Retest SAS Scores in Verbal Reasoning, Abstract/Visual Reasoning, and Short-Term Memory in Children with FRAXA and Autism

SAS		Factor	df	Mn.Sqr	F-ratio	Sig. Level
Verbal Reasoning	Within Ss					
		Time	1	1370.8	45.45	<<.001
		Time w/in Group	1	203.4	6.74	<.01
		Residual	32	30.2		
	Between Ss					
		Group	1	1840.6	10.42	<.003
		Cohort	1	653.5	3.70	~.06*
		Residual	32	176.7		
Abstract/Visual	Within Ss					
		Time w/in Cohort	1	331.6	4.54	<.04
		Time w/in Group	1	333.5	4.57	<.04
		Residual	32	73.0		
Short-term Memory						
	Within Ss					
		Time	1	309.9	4.44	<.04
		Time w/in Cohort	1	253.3	3.63	~.07*
		Residual	32	69.8		
	Between Ss					

		CohortXGroup	1	567.5	3.0	~.10*
		Cohort	1	722.5	3.82	~.06*
		Residual	32	189.2		

*Marginal significance
Factors not shown in the table were not statistically significant.

Table 3. Repeated Measures Analysis of Adaptive Behavior Composite Scores, Communications Domain, Daily Living Skills, and Socialization Domain Scores for Children with FRAXA and Autism.

Adaptive Behavior		Factor	df	Mean Sq.	F-Ratio	Sig. Level
Composite	Within Ss					
		Time	1	1515.0	24.51	<<.001
		Residual	32	61.8		
	Between Ss					
		Group	1	4023.4	13.05	<.001
		Residual	32	308.2		
Communication Domain	Within Ss					
		Time	1	1548.0	17.27	<<.001
		Residual	32	89.65		
	Between Ss					
		Group	1	2887.2	8.84	<.006
		Cohort	1	1286.3	3.94	<.05
		Residual	32	326.7		

Table 3 (Continued)

Adaptive Behavior		Factor	df	Mean Sq.	F-Ratio	Sig. Level
Daily Living Skills	Within Ss					
		Time	1	4281.5	35.65	<<.001
		Residual	32	120.1		
	Between Ss					
		Group	1	4669.2	9.61	<.004
		Cohort	1	2066.4	4.26	<.05
		Residual	32	485.7		
Socialization Domain	Within Ss					
		Time	1	907.3	8.99	<.005
		Residual	32	100.9		
	Between Ss					
		Group	1	8945.1	27.57	<<.001
		Residual	32	324.5		

Factors not shown in the table were not statistically significant.

Figure 1. Composite IQ Scores for Children and Adolescents with Fragile X or Autism

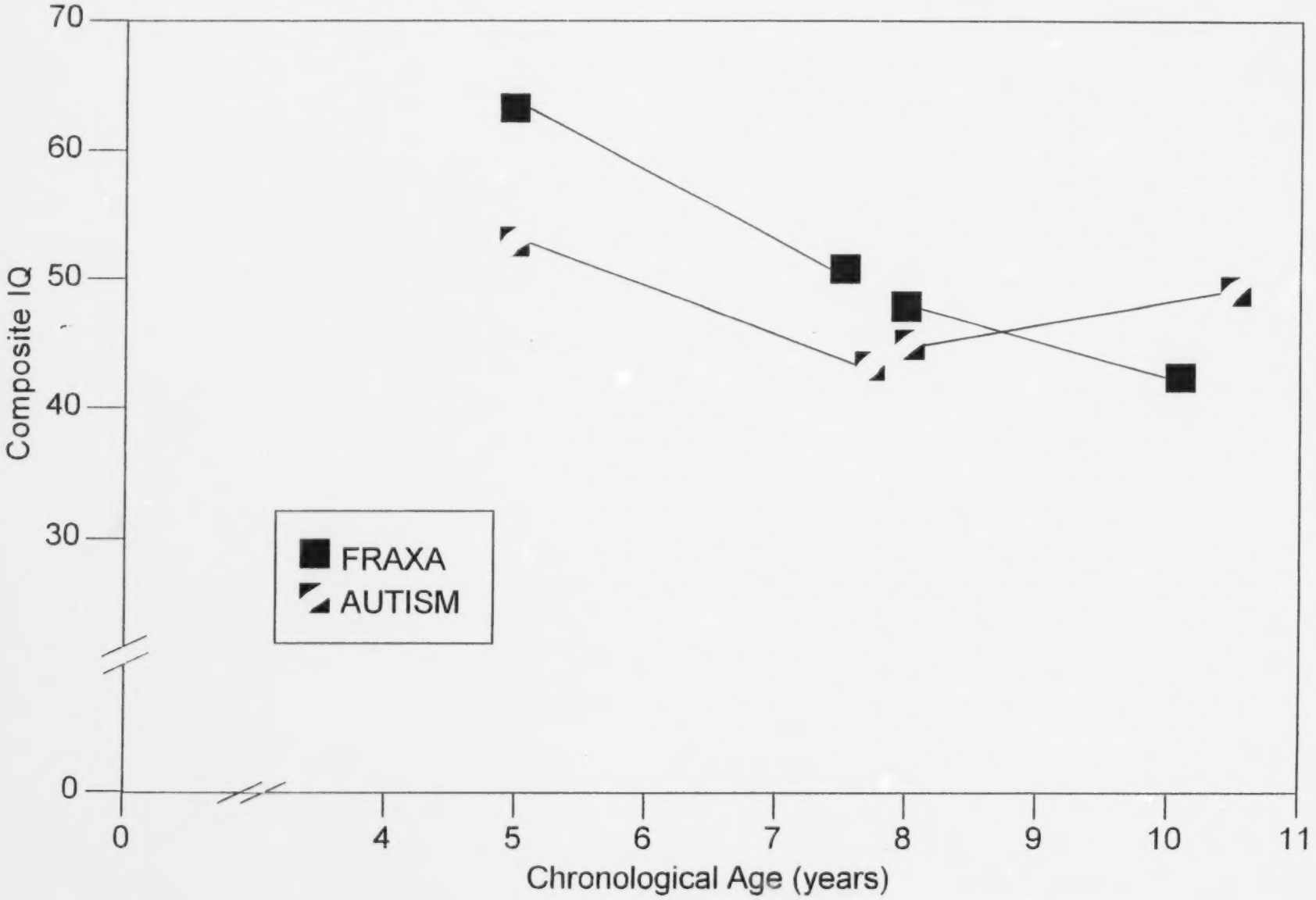

Figure 2. Adaptive Behavior Composite Scores for Children and Adolescents with Fragile X or Autism